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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	10

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,370	MAILLIET ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-31 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-31, wherein the distribution agent is a triazine in Paper No. 9 is acknowledged.

However, as pointed out by the applicants and upon further consideration, examiner noted omission and additional group V that is meant to cover subject matter not covered in invention I-IV. Hence a revised restriction requirement as shown below is made.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2 and 4-31, drawn to compound of general formula shown in claim 1 wherein the distribution agent is a triazine or formula I, composition and method of use, classified in class 544, subclasses 180, 196, class 514, subclasses 241, 242.

II. Claims 1-7 and 27-31, drawn to compound of general formula shown in claim 1 wherein the distribution agent is a pyrimidine or quinazoline, composition and method of use, classified in class 544 subclasses 283, 284, class 514, subclasses 256, 258.1.

III. Claims 1, 4-7, and 27-31, drawn to compound of general formula shown in claim 1 wherein the distribution agent is not a triazine or diazine and the nitrogen containing aromatic ring is quinoline or pyridine, composition and method of use, classified in class 546 subclasses 152, 268.1, class 514, subclasses 311, 345.

IV. Claims 1-2, 4-, and 27-31, drawn to compound of general formula shown in claim 1 wherein the distribution agent is a pyrimidine or quinazoline, and the nitrogen containing aromatic ring is not quinoline or pyridine, composition and method of use, classified in classes various subclasses various depending upon the choice of nitrogen containing group and the distribution group. If group IV is elected applicants should elect specific nitrogen containing aromatic ring and a specific distribution group for examination.

V. Claims 1-2, 4-, and 27-31, drawn to compound of general formula shown in claim 1 not provided for in invention I-IV, composition and method of use, classified in classes various subclasses various depending upon the choice of nitrogen containing group and the distribution group. If group V is elected applicants should elect specific nitrogen containing aromatic ring and a specific distribution group other than those recited in invention I-IV for examination.

The inventions are distinct, each from the other because of the following reasons:

Invention I, II, III, IV and V are independent and distinct from each other because they are directed to structurally dissimilar compounds that lack common core namely isomeric triazines versus pyrimidine or quinazoline versus isomeric diazines versus pyridine or quinoline versus nitrogen-containing aromatic groups. Consequently, the groups have different classifications and require separate prior art searches. They can be made and used independently. Art, which may render obvious or anticipate one of the groups would not necessarily do the same for the other group. Each can support a patent, as the compounds of each group are capable of being utilized alone not in

combination with other members listed in the Markush group. In addition, it is necessary to classify and search all the hetero cores and such a search of all cores would serious search burden given the limited time available for each application.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention: quinoline, pyridine, pyrimidine, generic diazines, benzamides and triazine. Searching all these groups is a serious search burden

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-31 generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Todd Rands on 7/11/2003 a provisional election was made with traverse to prosecute the invention of I, claims 1-2, and 4-31. Affirmation of this election must be made by applicant in replying to this Office action. Claim 3 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-2 and 4-31 will be examined to the extent they embrace the elected subject matter.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i). The traversal is on the ground(s) that it is not serious burden search and the instant invention has common structural element.

Applicants' traversal of earlier restriction requirement in paper # 9, is fully considered but deemed as not persuasive for reasons of record. As for the traversal the following apply.

1. First of all, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 - § 806.05(i)); and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) - § 806.04(i), § 808.01(a), and § 808.02).

Both these criteria are to be met with.

Contrary to applicants' urging, both the criteria of distinct and independent invention and search burden are clearly presented in the previous office action. To summarize, principles of classification dictate that ring structures with different ring sizes and having different numbers of heteroatoms to be classified in different classes. Such classification, as noted in the previous office action, stems from the fact that the ring structures have different properties, different reactivities and different effects on the substituents. They are made and used differently. In the instant case, the there are several hetero rings embraced in the instant claims such as, diazines(generic) triazines(generic), pyrmidines, quinazoline, pyridine, and heterocyclics (generic in addition to aromatic core such as benzamidine. Hence each invention is distinct and independent. Furthermore, applicants have not asserted that the core groups are all equivalent. In which

case, prior art, which anticipates instant elected invention, may then render the non-elected inventions as obvious variant and can thus be applied.

2. Applicants' argument that there is no serious search burden to examine all said groups is totally incorrect. First of all, as noted above, they are directed to structurally dissimilar compounds that lack common core. Consequently, the groups have different classifications and require separate prior art searches. It is mandatory for the examiner to search all classes and subclasses. Contrary to applicants' urging it would not be possible with the limited fixed time available for the examiner to examine each case with thorough search. Searching all possible classes and subclasses embraced by the generic and specifically recited core would of serious search burden.

3. Examiner also noted in the previous office action "Should applicant traverse on the ground that the core species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention". Applicants have not asserted that the two groups are not distinct. Applicants have not submitted evidence or identified such evidence now of record showing the core group to be obvious variants or clearly admitted on the record that all core groups embraced in the instant inventions are equivalent. In which case examiner needed not search all cores. A prior art which anticipates

any one of the groups embraced by a specific core (i.e. choices of I, II,III) may then render rest of the core groups as obvious variant. In other words, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

In want of such assertion or evidence, searching the entire core would be serious search burden given the limited time available for examining each case.

The restriction requirement is still deemed proper.

Claims 1,2, and 4-31 are now under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, and 4-31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. In claim 1, recitation of "thio radical" and "oxy radical" renders the claim indefinite and vague as "thio" and " oxy" are divalent entity. Replacement of these groups with "thiol" and "hydroxy" is suggested. See also claims 5, 9, and19.
2. Claims 5-26 recite " compounds" which implies the claims embrace a mixture of compounds not to single individual compound as recited in claim 1 on which these are dependent. An appropriate correction/clarification is needed.

3. Claims 16, 17, and 27 provide for the use of compound of claim 1 as pharmaceutical, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

4. The composition claim 30 is indefinite as it recites "radiation " as part of the composition. It is not clear how radiation per se is to be included in a therapeutic composition.

5. The method of use claim 31 lacks therapeutically effective amount.

6. In claim 18 recites "Novel" which lacks support and in claim 1, entry 2, subscript for R_3 is missing. An appropriate correction is requested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 4-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "thiol' and "hydroxy" or amino radical as substituents in the triazine, does not reasonably provide enablement for thio radical substituted with halogen, oxy radical substituted with halogen or amino radical substituted with halogen as recited for compound of claim 1 The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Note dependent claims 2, and 4-31 are also rejected herein as they depend on the rejected claim 1.

In evaluating the enablement question, following factors are considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

   The invention is drawn to compound of formula shown in claim 1 wherein the distribution group is triazine. Claim permits halogen substituents on "thio" or "oxy" or "amino" radical in presence of similar reactive groups on the quinoline or benzamidine or nonaromatic hydrocarbon chain. Specification is not adequately enabled as to how to make compounds of formula shown in claim 1 wherein the above said groups are variously substituted with reactive functional groups such as HO, NH_2, amidine and thiol groups which are also susceptible to halogenation.

   Specification offers no teachings or suggestion as to how to perform the halogenation and make such compounds in presence of these reactive groups.

2. The predictability or lack thereof in the art:

   The process of halogenation as applied to the above-mentioned compounds claimed by the applicant is not an art-recognized process and hence there should

be adequate enabling disclosure in the specification with working example(s) to make these claimed compounds.

4. The amount of direction or guidance present:

Examples illustrated in the experimental section or written description offer no guidance or teachings as to how make these compounds when reactive substituents or chemically incompatible substituents are present in the starting material.

5. The presence or absence of working examples:

Although examples on pages 28-37 show enablement for number of compounds, they are limited to compounds with no reactive functionality. There are no representative examples showing the viability of the process for the reactive thiohalo, oxyhalo, or aminohalo substituents embraced in the instant claims.

6. The breadth of the claims:

Specification has no support, as noted above, for all compounds generically embraced in the claim language would lead to desired compound of formula I with said reactive groups and there is also no valid chemical reasoning for one trained in the art to expect that all these functional groups would be inert toward the reaction to make such thiohalo, oxyhalo, or aminohalo compounds.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of

experimentation, there is no guarantee that one would get the product of desired structure, namely compound of formula shown in claim 1 in view of the general reactive of thiohalo, oxyhalo, or aminohalo groups.

Thus, factors such as "sufficient working examples", the "level of skill in the art and predictability, etc. have been demonstrated to be sufficiently lacking in the case for the instant claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16, 17, and 27 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-9, 11-15, 17-27, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daeyaert et al US 6,150,360.

1. Determining the scope and contents of the prior art.

Daeyaert et al. teaches several trisubstituted triazines, which include generically compounds of claimed in the instant claims, for the treatment of HIV infection. See formula I on col. 1, lines 30-40 and note the definition of L, A, R^1, R^2, R^3 and R^4 and n. Note with these definitions, compounds taught by Daeyaert et al. corresponds to instant triazine with pyridine as nitrogen containing aromatic ring

and L as nonaromatic hydrocarbon chain groups. See col. 2 through 9 for preferred embodiments and examples of the compounds on col. 9-10, process of making and compounds made on col. 10 through col. 22. See col. 23 to 27 for compounds made, especially see Table 2 and Table 3.

2. **Ascertaining the differences between the prior art and the claims at issue.**

Instant claims differ form the reference in reciting specific substituent pyridine in the triazine ring.

3. **Resolving the level of ordinary skill in the pertinent art.**

However Daeyaert et al. teaches the equivalency exemplified examples of trisubstituted core, shown on col. 9 and Table 2 and Table 3 with those claimed therein in the definition of various variable groups of formula I on col. 1. See definition of L, A, R^1, R^2, R^3 and R^4 and n shown on col. 1-2 and preferred embodiments of these groups on col. 2-9.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted the triazine ring as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

4. **Considering objective evidence present in the application indicating obviousness or nonobviousness**

The application does not offer any unexpected /superior results or any objective evidence that would suggest the instant invention is not an obvious variant.

References cited in the Information Disclosure Statement (paper # 1) are made of record.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM.

The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

7/9/2003